Critique of "Quantifying the effects of promoting smokeless tobacco as a harm reduction strategy in the USA" by Mejia AB, Ling PM, Glantz SA. Tobacco Control 2010

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ABSTRACT

When data are lacking, models that simulate population health events under different exposure scenarios may serve to inform policy by providing the basis for decision making. In order to be used in this manner, the underlying assumptions must be realistic, and the data used to define the starting point, or “base case”, must be accurate.

Methods: We assessed a recently published model, and evaluated its utility as a tool to estimate the effectiveness of tobacco control policy by: (1) critiquing the assumptions underlying the model and its input data; (2) comparing the published model estimates with estimates developed using the model as described, but with more realistic input data; and (3) using the original input data in a more realistic model, and comparing those results to the published model estimates.

Results: The proposed model is overly simplistic and sensitive to small changes. The data selected for input into the model produced similar results when used in a similar model, but use of only slightly more realistic input data or model assumptions resulted in entirely different conclusions about the likely effect of the policy under consideration.

Conclusion: The proposed model contains errors that must be corrected. At present, it does not provide information useful for evaluating or setting tobacco control policy.

INTRODUCTION

When data are lacking, models that simulate population health events under different exposure scenarios may serve to inform policy by providing the basis for decision making. In order for models to be used in this manner, their underlying assumptions must be as realistic as possible, and the data used to define the starting point, or "base case", must be accurate. If these criteria are met, then using the model to describe the potential effects of extreme scenarios (i.e., "worst case" and "best case") can provide useful information about the magnitude of effects to be expected for more reasonable scenarios.

In a recent publication, Mejia et al. described a model using Monte Carlo simulations, to evaluate the population level health effect that might be expected if smokeless tobacco products were successfully promoted in the US as a safer alternative to cigarettes, resulting in substantial changes in the patterns of use of tobacco products (Mejia, Ling, et al. 2010). The authors concluded that "promoting smokeless tobacco as a safer alternative to cigarettes is unlikely to result in substantial health benefits at a population level". We investigated the methods described by Mejia et al. (2010), and evaluated their conclusion using three approaches: 1) critiquing the assumptions underlying the model and its input data; (2) comparing the published model estimates with estimates developed using the model as described, but with more realistic input data; and (3) using the original input data in a more realistic model, and comparing those results to the published model estimates. We used the results of this investigation to evaluate the utility of their model for policy-making purposes.

CRITIQUE OF MODEL ASSUMPTIONS AND INPUT DATA

Model transitions

Mejia et al. (2010) describe their model as beginning with a hypothetical population of non-users of tobacco who are then allowed a very limited number of possible transitions between exposure states.

People are allowed to initiate cigarette smoking or smokeless tobacco products, cigarette and smokeless tobacco initiators are allowed to continue use, quit use; switch to the other product, or to become users of both products ("dual users"). Return to cigarette smoking or smokeless product use after cessation, switching from continued cigarette use to a smokeless product or switching from continued smokeless product use to cigarette smoking are not modeled. The model also does not allow non-users of tobacco to initiate cigarette smoking.

Transition probabilities

A crucial aspect of any model-based evaluation of the effectiveness of a health policy is the model input. Any data selected for the model, and the rationale for their selection, must be clearly documented for the model to be useful in evaluating the potential effectiveness of a proposed policy. In the tobacco harm reduction arena, model results depend heavily on the transition probabilities selected to describe movement between different tobacco exposure states that are expected to result from policy changes. For their base case scenario, Mejia et al. estimated transition probabilities based on multiple populations that differed with respect to age, calendar year and region, even though patterns of tobacco use have been shown to depend strongly on these factors (e.g. (CDC 2007; Gilpin, Pierce, et al. 1992; Nelson, Mowery, et al. 2006; Roth, Roth, et al. 2005; Tomar 2003). The estimated probabilities were applied to the entire hypothetical population, and did not account for age or gender. In addition, some transition probabilities were based on the estimated lifetime prevalence of ever use, others on the prevalence of current use, and yet others on the 2-year incidence of initiation, even though incidence and prevalence are not interchangeable measures or concepts.

- he incidence of *smokeless product initiation* (4%) was based on the arithmetic average of: the prevalence of smokeless product use among adults in 2005 based on the National Survey on Drug Use and Health (3.3%) (NSDUH 2005); the prevalence of smokeless product use among adults (2.3%) based on data from the National Health Interview Survey (NHIS) conducted in 2000 (Nelson et al., 2006); and the prevalence of smokeless product use among 9-12th graders in 2003

(6.7%) based on NHIS data (Nelson et al., 2006). Mejia et al. (2010) averaged these prevalence estimates without taking the differences between the source populations into account.

- o estimate transition probabilities *from smokeless tobacco use to other exposure states*, Mejia et al. used data from Oregon boys in grades 7 and 9 who were followed for 2 years in the late 1990s. The implicit assumption was that the hypothetical population of smokeless product "initiators" (which in their example was the population of current smokeless product users) was like Oregon 7th and 9th grade boys in terms of their tobacco use patterns.

- The incidence of *cigarette smoking initiation* was assumed to be equal to the lifetime prevalence of ever smoking among US adults in 2006 (40%). Mejia et al (2010) then divided the group of cigarette "initiators" (i.e., ever smokers in 2006) into categories of continuing smokers, quitters, smokeless product users and dual users based on their motivation to quit smoking in future. The transition probabilities were chosen such that "the end state reflected the current smoking and smokeless use prevalence and quit ratio in the 2006 NHIS survey" (page 298), although the NHIS 2006 survey data were not used by Mejia et al. to provide estimates of smokeless use. The end state distribution of continuing smokers and quitters was approximately even (47% and 53%, respectively) based on the NHIS estimate that 50% of current smokers were able to quit smoking.

Discussion of the motivation to quit smoking in the future (will never quit; is health concerned; is affected by smoke-free regulations; and is price sensitive) comprised a substantial part of the Mejia et al. paper. However, motivation to quit is irrelevant to the stated purpose of the model, which was to estimate the population-level health effect to be expected under different distributions of cigarette smoking and smokeless tobacco use. The proportions of subjects in each motivation category were reportedly based on a study of adult smokers who had smoked for

at least 5 years in 1987 (Gilpin, Pierce, et al. 1992). This cross-sectional study used data from the 1987 NHIS and reported the distribution of reported reasons for quitting smoking in the past 5 years among former smokers, and not motivation to quit smoking in the future among current smokers. The Gilpin et al. study did not consider a "smoke-free environment" category, it included a "health concerned *and* price sensitive" category because of considerable overlap between the two categories among their respondents, and it included several additional categories not considered by Mejia et al. (e.g., "lost interest" and "miscellaneous", among others). The proportion of the population of former smokers reporting reasons for quitting smoking that were not considered by Mejia et al. was almost 50% in the Gilpin et al. (1992) data. Further, according to Gilpin et al., the proportion of subjects that had never tried to quit smoking was 18% among ever smokers and 33% among current smokers, values that are very different from the 10% estimated by Mejia et al. (2010).

- inally, Mejia et al. calculated the probability of *remaining a non-user of tobacco* (56%) as the remainder after accounting for the 40% of the population identified as smoking "initiators" and the 4% of the population identified as smokeless tobacco "initiators". The model allowed cigarette "initiators" (i.e., ever smokers) and smokeless product "initiators" (i.e., current users) to transition to other tobacco exposure states, but those initially defined as non-users of tobacco were not allowed to transition into tobacco use.

Tobacco-related health effects

Mejia et al. created an artificial "tobacco-related health effects" variable to place the different tobacco exposure categories on a continuum of risk, where non-users of tobacco were at zero, former smokers, current smokeless product users and current dual users were log-normally distributed with means of 5, 11 and 90, respectively, and smokers were at 100. References to justify these values were only provided for smokeless product users; even in this case, the value of 11 (standard deviation = 5) was not directly

derived from data but was a consensus estimate. Neither duration of use nor cessation was considered in estimating tobacco-related health risk.

Scenarios and results

Mejia et al. modeled a number of scenarios to represent different levels of adoption of smokeless tobacco products due to varying hypothetical levels of successful smokeless product promotion. The modeled results under each of the scenarios produced wide posterior intervals that overlapped with one another and the base case scenario, indicating that none of the point estimates could be interpreted as demonstrating statistically significant differences in health risk resulting from differences in the exposure distributions. Under the "aggressive smokeless promotion" scenario considered by Mejia et al. to be the most extreme example, the transition probabilities and other assumptions in the model (e.g. that half the smokeless product users came from never tobacco users) were so unrealistic that even though a much lower health risk was assumed for smokeless product users than for cigarette smokers, the model suggested (statistically non-significant) net harm at the population level.

Mejia et al. acknowledged that their transition probabilities were less than ideal, but claimed that better data were unavailable. However, we found several examples that could have been used: Lundqvist et al. reported on patterns of tobacco use in a population of middle-aged Swedes that included initiation, cessation and rates of transition among cigarettes, smokeless tobacco and dual use over a ten year period (Lundqvist, Sandstrom, et al. 2009). Transitions between exposure states among adults in the United States, including cessation of smokeless tobacco and dual use, were provided by Zhu et al. in analyses of the Current Population Survey-Tobacco Use Supplement for 2002 and 2003 (Zhu, Wang, et al. 2009). Smoking initiation rates are available from the National Health Interview Survey (Escobedo and Peddicord 1997). The National Survey on Drug Abuse provides estimates of smoking initiation in the US (Office of Applied Statistics, 1998 and 1999); its successor, the National Survey of Drug Use and Health, provides estimates of cigarette and ST initiation for people aged 12 and older as recently as 2008 (http://oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf); and Davis et al. provided estimates of smoking initiation specifically for youth smokers (Davis et al., 2009). The study of Oregon teenagers that Mejia et al. relied on for smokeless tobacco product transition rates (Severson, Forrester, et al. 2007) also

reported the probability of cigarette and smokeless tobacco initiation and the transition probabilities for those who used smokeless products at baseline, but these estimates were not used by Mejia et al.

From these alternative sources, we selected the three papers (Lundqvist et al., 2009; Severson et al., 2007 and Zhu et al., 2009) that provided the most complete sets of initiation, cessation and transition probabilities for comparison with the data used by Mejia et al. (2010). Compared to the probabilities presented by Lundqvist et al. (2009) for Swedish adults and the probabilities observed by Severson et al. (2007) among teenage boys in Oregon, Mejia et al. considerably underestimated the proportion of persons remaining non-tobacco users and greatly overestimated the smoking initiation probability among non-tobacco users (table). The estimate used by Mejia et al. (2010) was similar to that provided by Escobedo and Peddicord (1997) based on data from the early 1980s, but greater than that provided by Davis et al. (2009) based on students in grades 6-12 who participated in the ALLTURS study between 2000 and 2002. Further, contrary to evidence reported by Zhu et al. and Lundqvist et al. (2009), Mejia et al. (2010) assumed that (i) cessation of use was much lower among smokeless product users than cigarette smokers while initiation of dual use was much higher among smokeless product users; and (ii) switching from one product to the other was much more common among smokeless tobacco users than cigarette smokers.

Table: Comparison between transition probabilities used by Mejia et al. (2010) and alternative transition probabilities published by others

Transition	**Mejia**	**Zhu**		**Severson**	**Lundqvist**	
Population	Hypothetical US any age	US adults		Oregon boys in grades 7 & 9	Swedish adults	
Duration of follow-up	-	1 year		2 years	10 years	
From no tobacco use to					M	F
No tobacco use (no change)	56%	-		72%	94%	97%
Smokeless tobacco	4%	-		5%	5%	1%
Cigarette smoking	40%	-		16%	1%	2%
Dual use	0%	-		8%	0%	0%
From smokeless tobacco to		M	F		M	F
No tobacco use	17%[1]	40%	47%	17%	19%	18%
Smokeless tobacco (no change)	26%[1]	59%	53%	26%	77%	79%
Cigarette smoking	17%[1]	4%	3%	17%	1%	0%
Dual use	40%[1]	2%	<1%	40%	3%	3%

From cigarette smoking to	B	A	M	F		M	F
No tobacco use	47%	44%	12%	12%	-	26%	33%
Smokeless tobacco	0%	8%	<1%	<1%	-	14%	8%
Cigarette smoking (no change)	53%	37%	86%	88%	-	53%	57%
Dual use	0%	13%	2%	0%	-	7%	2%

[1] from Severson et al, 2006
B = Baseline scenario
A =“Aggressive promotion” scenario
M = Males
F = Females

Model validation

Mejia et al. did not report any attempt to validate their model, although they did successfully replicate results, using similar model input, produced by another technique (Gartner, Hall, et al. 2007). Some problems underlying the model whose results Mejia et al. chose to replicate have been discussed elsewhere (Sulsky, Bachand et al., 2010)

SENSITIVITY ANALYSIS

Having identified problems with the data selected as model input by Mejia et al., we attempted to assess the model assumptions by using more defensible input and evaluating the difference in results. Although the authors provided the full model input, via a spreadsheet accessible to journal (Tobacco Control) subscribers through its web site, the spreadsheet does not perform any calculations. However, we had already used the WinBUGS computer program to create a simulation model that estimates mortality or morbidity for a hypothetical population of persons who have never used tobacco and who, as they age, may transition into and out of 33 possible tobacco exposure states, including current and former smoking or smokeless product use and recidivism for those who had quit. A brief description of this model is available (Bachand, Curtin, et al. 2010); a full description is currently being prepared for peer review. We were able to use the data documented in the spreadsheet provided by Mejia et al. in a simplified form of our simulation model to replicate their results. We then tested the sensitivity of their model by modifying the input documented by Mejia et al. and using it in the simplified form of our model.

Alternative results

We simplified our model to restrict it to the transitions described by Mejia et al. (2010). After cigarette smoking initiation, only one change in tobacco exposure was allowed, and only one change was allowed after smokeless product initiation unless the subject switched to cigarettes; in this case, one additional change could be made. For transitions not modeled by Mejia et al., we used transition probabilities of 0.

Using the model input specified by Mejia et al. (2010) was difficult to accomplish for several reasons: (i) Mejia et al. did not take age into account, while our model does; (ii) We did not use prevalence as an estimate of incidence in our model. Whenever their transition probabilities were prevalence estimates, we used incidence estimated from the National Household Survey on Drug Abuse (Office of Applied Studies, 1999), instead; and (iii) The proportions used by Mejia et al. to describe the distribution of motivations to quit were not useful for the stated purpose and were not based on reliable information; therefore, we calculated the weighted average of their transition probabilities for each of the four end states: quitting, continuing cigarette use, switching to a smokeless product and dual use.

For this example, we used Mejia et al.'s comparison of the "aggressive smokeless promotion" scenario to their base case scenario. To approximate the input used by Mejia et al., we kept the ratios between the transition probabilities the same as the ratios between the "aggressive smokeless promotion scenario" and the transition probabilities in their base case scenario. It is important to keep in mind that their base case scenario assumed that 4% of the population used smokeless products while we assumed no form of tobacco use at baseline, but allowed proportions of the population to initiate cigarette or smokeless tobacco use at user-defined, age-specific rates.

In our analysis, follow-up started at age 13, the youngest age at which a non-negligible proportion of tobacco users initiates use, and ended at age 72. The width of each age category was five years. To allow for validation of the model results against current mortality data accounting for adequate disease induction time, we based age category-specific smoking initiation rates on the 1980 National Household Survey on Drug Abuse (Office of Applied Studies, 1999). Age category-specific smoking cessation rates for 1980 were based on data from *The California Tobacco Control Program's effect on adult smokers: (1) Smoking cessation* (Messer K et al., 2007). More recent data could be used to model prospective future population health effects, if desired. For smoking initiation, we used 11.25%, 10%, 1.25% and 0.25% for age categories 13-17, 18-22, 23-27and 28-32 years, respectively, and 0 for older age categories. For smoking cessation, we used 2.5% for age 13-17, 4.5 for the next 3 age categories, 5.0 for category 33-37 years, 5.5 for categories 38-42 and 43-47 years, 7.5% for category 48-52 years and 8.5% for the remaining 4 age categories.

Mejia et al. used tobacco use patterns reported by 145 7th and 9th grade boys to estimate the transition probabilities for the whole population following the use of a smokeless product. Therefore, we also used the transition probabilities reported for the 7th and 9th grade boys for all ages in our model.

Our model uses age-, years of smoking- and years of quitting-specific mortality rates based on the coefficients from a Poisson model estimated using data for men from the Kaiser Permanente Cohort study (Friedman, Tekawa, et al. 1997). The ratio of excess risks for current smokeless tobacco users versus smokers (0.08) was based on a consensus estimate reported by Levy et al. (Levy, Mumford, et al. 2004), and the ratio of excess risks for former smokeless product users versus smokers was set to 0.05. While Mejia et al. combined men and women in their analysis, we restricted our analysis to men because tobacco use patterns vary considerably between genders (see paragraph two of "Limitations", page 303 in Mejia et al. and reference numbers 5, 6, 12, 22, 29, 30, 31, and 36 from Mejia et al.).

Using data that replicated, as closely as possible, the flawed input and transition probabilities used by Mejia et al. to define a "worst-case" scenario of aggressive smokeless tobacco promotion, we, like them, observed statistically non-significant net harm. That is, there were more deaths estimated at the end of follow-up under the test scenario compared to the base-case, but the difference was not statistically significant.

We then made a slight change in the transition probabilities, such that the probabilities for transitions from smokeless tobacco use reported by Severson et al. for 7th and 9th grade boys were applied only to the youngest two age categories (13-<18 and 18-<23 years). For all other age groups, we used the transition probabilities reported by Lundqvist et al. or by Zhu et al. This change resulted in statistically significant net benefit , i.e., there were fewer deaths estimated at the end of follow-up under the test scenario compared to the base-case. Thus, running the model with only slightly more realistic input produced statistically significant estimates that suggested a benefit of aggressive smokeless tobacco promotion, rather than harm, at the population level.

As described above, the model used by Mejia et al. incorporated a very limited number of possible transitions between exposure states. Therefore, we wanted to determine the effect of using the flawed transition probabilities suggested by Mejia et al., but allowing all possible transitions in our model.

For transitions not modeled by Mejia et al., we assumed that transition probabilities for "no change in tobacco use" were 95%, while transition probabilities for "changes in tobacco use" were 5%; when more than one type of change was possible, the transition probability of 5% was divided between them. For example, the probability of remaining a cigarette smoker (no change) after several previous changes in tobacco use was set to 95% while the probability of switching back to a smokeless product and the probability of quitting were set to 2.5% each. We repeated the analysis allowing a 25% probability for "change in tobacco use" while the transition probabilities for "no changes" were 75%.

Allowing for a small degree (5%) of recidivism and switching from one to the other product after previous changes in tobacco use (while using Mejia et al.'s input, to the extent possible, for transitions considered in their model), we observed a net benefit (i.e., a reduction in mortality) at the population level. The benefit was statistically significant, based on the 95% posterior intervals, even when the transition probabilities for the 7^{th} and 9^{th} grade boys were applied to all ages. Allowing for a greater degree (25%) of recidivism and switching from one to the other product resulted in an even more pronounced, statistically significant, population benefit.

DISCUSSION

The model proposed by Mejia et al. model is overly simplistic in its use of only a limited number of exposure states and transitions: 56% of the starting population, identified as non-tobacco users at baseline, are not allowed to become tobacco users; no one who quits tobacco use is allowed to revert to a tobacco use state; the model uses the same initiation, cessation and transition rates for the whole hypothetical population, regardless of age or gender; and, the risk of tobacco related health outcomes "measured" by the health index is assumed to be the same regardless of duration of tobacco use or cessation.

The sources used by Mejia et al. (2010) to define the initial exposure distribution and the transition probabilities are difficult to justify. The authors mixed estimates for adult men and women, drawn from a nationally representative sample of current and former smokers, and for 145 7th and 9th grade boys who attended secondary school in one of a few towns in Oregon. The transition probabilities used by Mejia et al. incorrectly implied that smokeless tobacco users were very unlikely to quit (a beneficial transition) and very likely to switch to smoking or to initiate dual use (harmful transitions) while smokers were very likely to quit or to switch to smokeless tobacco (beneficial transitions) and unlikely to initiate dual use (a harmful transition).

The health index is of questionable validity, and does not seem to be based on empirical data. The data purportedly used to justify the values assigned to the health index comprised a mix of diseases and causes of death, measures of effect (incidence and prevalence), and exposures (product types). Furthermore, the Mejia et al. model assumes that risks associated with each type of tobacco product are the same for all users, i.e., the risk of experiencing a tobacco-related health outcome "measured" by the health index is assumed to be the same for males, females, all ages, and any duration of use or former use of tobacco.

The results reported by Mejia et al. did not indicate statistically significant differences between exposure groups, yet the authors interpreted the results as showing no benefit of smokeless tobacco. An objective interpretation of their results is that the model provides no evidence for either benefit or harm to the population associated with increased promotion of smokeless tobacco use.

Due to the significant shortcomings of the methods employed by Mejia et al., their conclusion that "promoting smokeless tobacco as a safer alternative to cigarettes is unlikely to result in substantial health benefits at a population level" does not follow from the results. Small changes to Mejia et al.'s model input or assumptions led to the opposite conclusion. Because of its flaws, the simulation model proposed by Mejia et al. does not provide information that can be used in evaluating or setting tobacco control policy.

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Competing interests: The authors are preparing an alternative tobacco harm reduction model for publication, and anticipate it will receive substantial and rigorous peer review.

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